ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylan 200, 200mg/ml Solution for Injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance
Tylosin (as the base) 200 mg/ml
Excipient
Benzyl Alcohol 40 mg/ml
For a full list of excipients see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A sterile yellow solution

4 CLINICAL PARTICULARS

4.1 Target Species

Tylan 200 mg/ml Solution for Injection is indicated for use in cattle and pigs.

4.2 Indications for use, specifying the target species

TYLAN 200 mg/ml Solution for Injection is indicated in all conditions associated with bacteria sensitive to tylosin which includes organisms in the following genera:

Streptococcus	Campylobacter
Bacillus	Spirochaetes
Staphylococcus	Chlamydia
Corynebacterium	Fusiformis
Clostridium	Pasteurella
Erysipelothrix	

TYLAN 200 mg/ml Solution for Injection has been successfully used in respiratory and genito-urinary tract infections, otitis, cellulitis and secondary bacterial conditions associated with virus disease or post-operative infections. Specific disease entities treated successfully with TYLAN include Swine Dysentery, Erysipelas and Enzootic Pneumonia in pigs, foul in the foot, mastitis and calf pneumonia in cattle.
For the treatment and metaphylaxis of enzootic pneumonia, swine dysentery and other scours caused by organisms sensitive to tylosin, in pigs.
For the treatment and metaphylaxis of pneumonia in cattle associated with mycoplasmata and *Pasteurella multocida* sensitive to tylosin.
The presence of the disease in the group must be established before the product is used.

4.3 Contraindications

Tylan 200 should not be given to chickens or turkeys.
Do not use in animals with known hypersensitivity to the active ingredients.
Do not use in equine animals.

4.4 Special warnings for each target species

None.

4.5 Special precautions for use

Special precautions for use in animals
Use of this product should be based on susceptibility testing of the bacteria isolated from the animal. If this is not possible, therapy should be based on local (regional, farm level) epidemiological information about susceptibility of the target bacteria. Whenever possible the product should only be used on the basis of susceptibility testing. Use of the product deviating from the instructions given in the SPC may increase the prevalence of bacteria resistant to tylosin and may decrease the effectiveness of treatment with other macrolide antibiotics due to potential of cross-resistance.
The efficacy data do not support the use of tylosin for the treatment of bovine mastitis caused by *Mycoplasma* spp.

Special precautions to be taken by the person administering the veterinary medicinal product to animals
Care should be taken to avoid accidental self-injection.

4.6 Adverse reactions (frequency and seriousness)

In very rare cases, the following adverse reactions have been observed in animals administered tylosin at the recommended rate:

- Injection site reaction
- vulvular swelling in cattle,
- oedema of the rectal mucosa, partial anal protrusion (rose budding), erythema and pruritus in pigs.
- anaphylactic shock and death.

Where repeat injections are to be administered, use different sites for each injection.

4.7 Use during pregnancy, lactation or lay

No adverse effects to tylosin have been seen in fertility, multi-generation or teratology studies.

4.8 Interaction with other medicinal products and other forms of interaction

None observed.

4.9 Amounts to be administered and administration route

Tylan 200 mg/ml Solution for Injection should be given by intramuscular injection at a dose rate of 10 mg/kg bodyweight.
The maximum injection volume for cattle is limited to 15 ml per injection site.
In pigs do not administer more than 5 ml per injection site.

The stopper of the veterinary medicinal product may be punctured up to a maximum of 30 times.

4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

Shock and death may occur on rare occasions following overdose in piglets and calves.

4.11 Withdrawal Period(s)

Cattle
Meat and offal: 28 days
Milk: 96 hours

Pigs
Meat and offal: 16 days
To avoid blemish at the site of injection pigs should not be slaughtered for human consumption for 21 days following last treatment.

5 PHARMACOLOGICAL or IMMUNOLOGICAL PROPERTIES

Pharmacotherapeutic group: Antibacterials for systemic use, Macrolides, Licosamides and Streptogramins. ATCvet Code: QJ01FA90

5.1 Pharmacodynamic properties

Tylosin is a macrolide antibiotic produced by a strain of *Streptomyces fradiae*. It exerts its antimicrobial effect by inhibiting protein synthesis of susceptible micro-organisms.
The tylosin spectrum of activity includes Gram-positive bacteria, and some Gram-negative strains such as Pasteurella, at concentrations of 16µg/ml or less.

5.2 Pharmacokinetic properties

Absorption: Following intramuscular injection, tylosin blood levels peak 1-2 hours post-injection. Duration of activity is approximately 12 hours.

Distribution, Biotransformation and Elimination: Tylosin levels of 1.4 to 1.6 and 2.2 to 6.7 µg/ml were recorded in serum and lung tissue respectively following intramuscular injection of 8.8mg/kg bodyweight in pigs. Measurable amounts of tylosin were still present in both serum and lung tissue at 12 hours post injection. Tylosin concentrations were greater in lung tissue than serum at all sample times.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Benzyl Alcohol
Propylene Glycol
Water for Injections

6.2 Major incompatibilities

Do not mix with other solutions, since this may cause precipitation of the active ingredient.

6.3 Shelf-life

Shelf-life of the veterinary medicinal product as packaged for sale: 18 months.
Shelf-life after first opening the immediate packaging: 90 days.

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and composition of immediate packaging

Carton containing 100 ml clear type II glass vials, each of which is sealed with a grey butyl rubber bung with alumini overseal, packed in a carton.

6.6 Special precautions for the disposal of unused veterinary medicinal products or waste materials derived from the use of such products

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

7 MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann-Strasse 4
27472 Cuxhaven
Germany

8 MARKETING AUTHORISATION NUMBER(S)

VPA 22020/033/001

9 DATE OF THE FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 1st October 1988
Date of last renewal: 20th February 2009

10 DATE OF REVISION OF THE TEXT

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGE

CARTON

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylan 200, 200 mg/ml Solution for Injection

2. STATEMENT OF ACTIVE SUBSTANCES

Formula
Each ml contains 200 mg of tylosin base activity in 50% propylene glycol with 4% benzyl alcohol.

Tylosin

3. PHARMACEUTICAL FORM

Solution for Injection

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Cattle and pigs

6. INDICATION(S)

FOR INTRAMUSCULAR USE IN CATTLE AND PIGS

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Dosage and Administration
Recommended for farm animal use only.
Inject intramuscularly only. A dry hypodermic needle and syringe should be used where possible. It is advisable to alternate the injection site when repeated daily doses are given.
Cattle and calves: 10 mg per kg body weight (1 ml per 20 kg) daily.
Pigs: 10 mg per kg body weight (1 ml per 20 kg) daily.

8. WITHDRAWAL PERIOD(S)

Warning
Animals must not be slaughtered for human consumption during treatment. Cattle must not be slaughtered for human consumption within 28 days of the last treatment. Milk for human consumption must not be taken from a cow during treatment. Milk for human consumption may be taken only after 96 hours from the last treatment.
Pigs: Meat and offal: 16 days.
Pigs should not be slaughtered for human consumption for three weeks after the last treatment to avoid blemish at the site of injection.

9. SPECIAL WARNING(S), IF NECESSARY

Do not use in animals with known hypersensitivity to the active ingredients.

Tylan 200 should not be given to chickens or turkeys.
Do not use in equine animals. Injection of Tylosin in equines has been fatal.

10. EXPIRY DATE

Expiry Date:

11. SPECIAL STORAGE CONDITIONS

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

FOR ANIMAL TREATMENT ONLY.

POM

TO BE SUPPLIED ONLY ON VETERINARY PRESCRIPTION

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
Germany

16. MARKETING AUTHORISATION NUMBER(S)

VPA 22020/033/001

17. MANUFACTURER'S BATCH NUMBER

Batch No:

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGE

100ml VIAL

1. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylan 200, 200 mg/ml Solution for Injection

2. STATEMENT OF ACTIVE SUBSTANCES

Tylosin
Formula
Each ml contains 200 mg of tylosin base activity in 50% propylene glycol with 4% benzyl alcohol.

3. PHARMACEUTICAL FORM

4. PACKAGE SIZE

100 ml

5. TARGET SPECIES

Cattle and pigs

6. INDICATION(S)

FOR INTRAMUSCULAR USE IN CATTLE AND PIGS

7. METHOD AND ROUTE(S) OF ADMINISTRATION

Dosage and Administration
Recommended for farm animal use only.
Inject intramuscularly only. A dry hypodermic needle and syringe should be used where possible .It is advisable to alternate the injection site when repeated daily doses are given.
Cattle and calves: 10 mg per kg body weight (1 ml per 20) daily.
Pigs: 10 mg per kg body weight (1 ml per 20 kg) daily.

Directions for Use
See enclosed leaflet

8. WITHDRAWAL PERIOD(S)

Warning
Animals must not be slaughtered for human consumption during treatment. Cattle must not be slaughtered for human consumption within 28 days of the last treatment. Milk for human consumption must not be taken from a cow during treatment. Milk for human consumption may be taken only after 96 hours from the last treatment.
Pigs: Meat and offal: 16 days.
Pigs should not be slaughtered for human consumption for three weeks after the last treatment to avoid blemish at the site of injection.

9. SPECIAL WARNING(S), IF NECESSARY

Do not use in animals with known hypersensitivity to the active ingredients.
Tylan 200 should not be given to chickens or turkeys.
Do not use in equine animals. Injection of Tylosin in equines has been fatal.

10. EXPIRY DATE

Expiry Date:

11. SPECIAL STORAGE CONDITIONS

Do not store above 25° C.
Avoid the introduction of contamination during use.
Shelf-life after first use of vial – 90 days.

12. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCTS OR WASTE MATERIALS, IF ANY

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

13. THE WORDS "FOR ANIMAL TREATMENT ONLY" AND CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE, IF APPLICABLE

FOR ANIMAL TREATMENT ONLY.

POM

TO BE SUPPLIED ONLY ON VETERINARY PRESCRIPTION

14. THE WORDS "KEEP OUT OF THE SIGHT AND REACH OF CHILDREN"

Keep out of the sight and reach of children

15. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Elanco GmbH,
Heinz-Lohmann-Str. 4
27472 Cuxhaven,
Germany

16. MARKETING AUTHORISATION NUMBER(S)

VPA 22020/033/001

17. MANUFACTURER'S BATCH NUMBER

Batch No.:

B. PACKAGE LEAFLET

PACKAGE LEAFLET:
Tylan 200, 200 mg/ml Solution for Injection

1. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER AND OF THE MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE, IF DIFFERENT

Marketing authorisation holder:
Elanco GmbH
Heinz-Lohmann-Str. 4
27472 Cuxhaven
Germany

2. NAME OF THE VETERINARY MEDICINAL PRODUCT

Tylan 200, 200 mg/ml Solution for Injection

3. STATEMENT OF THE ACTIVE SUBSTANCE(S) AND OTHER INGREDIENT(S)

Tylosin
Tylosin is an antibiotic fermentation product of a soil isolate closely resembling *Streptomyces fradiae*, which was isolated in the Lilly Research Laboratories from a soil sample collected in Thailand.
Presentation
A sterile yellow aqueous solution of tylosin base in 50% propylene glycol with 4% benzyl alcohol.
Each ml contains 200 mg of tylosin activity (as tylosin base).

4. INDICATION(S)

FOR INTRAMUSCULAR USE IN CATTLE AND PIGS
Recommended for the farm animal use only.
Properties
Tylan 200 possesses a wide spectrum of antibiotic activity against micro-organisms.
Particularly active against Gram-positive bacteria, it is also effective against several species of spirochaetes, Chlamydia and certain Gram-negative bacteria.
Tylan 200 is indicated in all conditions associated with bacteria sensitive to tylosin which includes organisms in the following genera:

Streptococcus	*Campylobacter*	*Fusiformis*
Bacillus	*Spirochaetes*	
Staphylococcus	*Corynebacterium*	
Clostridium	*Pasteurella*	
Erysipslothrix	*Chlamydia*	

Tylan 200 has been successfully used in respiratory and genito-urinary tract infections, otitis, cellulitis and secondary bacterial conditions associated with virus disease or post operative infections.
Specific disease entities treated successfully with Tylan 200 include: Swine Dysentery, Erysipelas and Enzootic Pneumonia in pigs, foul in the foot, mastitis and calf pneumonia in cattle.
For the treatment and metaphylaxis of enzootic pneumonia, swine dysentery and other scours caused by organisms sensitive to tylosin, in pigs.
For the treatment and metaphylaxis of pneumonia in cattle associated with mycoplasmata and *Pasteurella multocida* sensitive to tylosin.
The presence of the disease in the group must be established before the product is used.

5. CONTRAINDICATIONS

CONTRA-INDICATIONS AND SIDE EFFECTS
For animal treatment only.
Do not administer to chickens or turkeys.
Do not use in animals with known hypersensitivity to the active ingredients.

Do not administer to horses or other equines. Injection of Tylosin in equines has been fatal.
As with the injection of any foreign substance, a reaction may occur in animals.
Since temporary irritation may occur at the site of injection in swine, it is suggested that a sufficient time interval be allowed before animals are slaughtered tor food.
To avoid blemish at point of injection, do not slaughter pigs within 21 days of administration.

6. ADVERSE REACTIONS

7. TARGET SPECIES

Cattle and pigs

8. DOSAGE FOR EACH SPECIES, ROUTE(S) AND METHOD OF ADMINISTRATION

Dosage and Administration

Inject intramuscularly only. A dry hypodermic needle and syringe should be used where possible .It is advisable to alternate the injection site when repeated daily doses are given.
Cattle and calves: 10 mg. per kg body weight (1 ml per 20 kg) daily.
Pigs: 10 mg. per kg body weight (1 ml per 20 kg) daily.
The maximum injection volume for cattle is limited to 15 ml per injection site.
In pigs do not administer more than 5 ml per injection site.

Caution

Avoid the introduction of contamination during use. Should any apparent growth or discolouration occur, the product should be discarded. The administration of antibiotics may result in the over-growth of non-susceptible organisms. If new infections due to bacteria or fungi appear during treatment with this drug, appropriate measures should be taken. If there is no response to therapy in 3 days, diagnosis and treatment should be reassessed.
Do not mix Tylan 200 for injection with other solutions, as this may cause a precipitation of the active ingredient.

9. ADVICE ON CORRECT ADMINISTRATION

The stopper of the veterinary medicinal product may be punctured up to a maximum of 30 times.

10. WITHDRAWAL PERIOD(S)

Cattle must not be slaughtered for human consumption during treatment or for at least 28 days after the last treatment.
Pigs: Meat and offal: 16 days.
Milk for human consumption must not be taken from a cow during treatment, milk for human consumption may be take only after 96 hours from the last treatment.

11. SPECIAL STORAGE PRECAUTIONS

Do not store above 25°C.
Keep out of the sight and reach of children.
Shelf-life after first use of a vial – 90 days.

12. SPECIAL WARNING(S)

Special precautions for use in animals:
The efficacy data do not support the use of tylosin for the treatment of bovine mastitis caused by *Mycoplasma* spp.

13. SPECIAL PRECAUTIONS FOR THE DISPOSAL OF UNUSED PRODUCT OR WASTE MATERIALS, IF ANY

Unused product or waste material should be disposed of in accordance with current practice for pharmaceutical waste under national waste disposal regulations.

14. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST APPROVED

15. OTHER INFORMATION

POM

Prescription medicine only.
To be supplied only on veterinary prescription.
VPA 22020/033/001

Tylan 200 is relatively non-toxic. The oral LD_{50} in mice is greater than 5 g per kg. Dogs have tolerated oral doses as high as 200 mg and 400 mg/kg for 657 days with only occasional side-effects, for example, vomiting and salivation. Overdoses of this nature have resulted in an occasional animal showing haematuria for several days. This was only evident some time after 20 to 190 days after administration.
In pigs, the LD_{50} by the intramuscular route is approximately 1 g per kg and by the oral route, greater than 5g per kg. Blood level studies have been conducted in cattle and pigs comparing Tylan 200 for injection to aqueous solutions of tylosin tartrate. A longer duration of activity was evinced with Tylan 200 for injection. Measurable blood levels of 22 hours duration can be expected in cattle with a single injection of the preparation at recommended doses. There has been no evidence of undue irritation in cattle at the site of injection. These studies, plus others in rats, chickens, pigs, cattle and calves further demonstrate the relative safety of this substance.